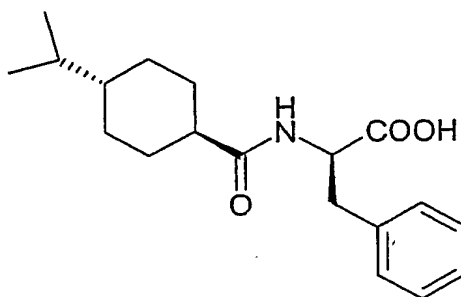


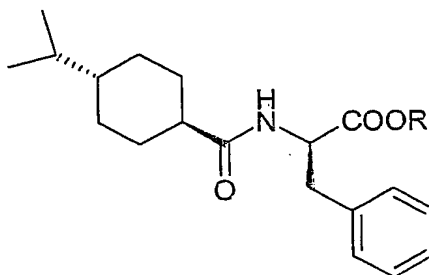
Claims:

1. A process for the preparation of crystalline modification "G" of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide) of the formula (I)



(I)

by treating a compound of the general formula (II)



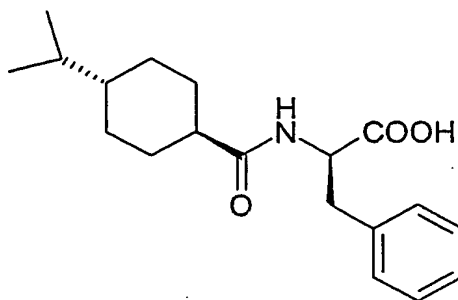
(II)

wherein R is a lower (C₁-C₄) alkyl group or hydrogen, with a base to yield an alkali salt, and liberating the product from said salt with an acid, characterized in that the acidic liberation of the product is carried out in a temperature range below room temperature, preferably in the temperature range of 0 °C to 20 °C.

2. A process according to claim 1, wherein a water-miscible organic solvent, preferably aqueous methanol, more preferably methanol containing 20-50 % water by volume is employed.

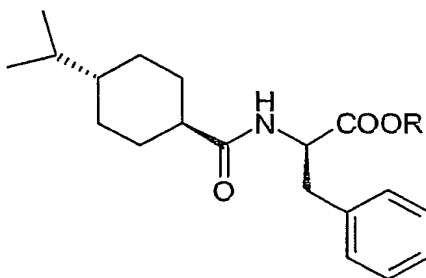
13

3. A process for the preparation of crystalline modification "H" of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide) of the formula (I)



(I)

5 by treating a compound of the general formula (II)



(II)

10 wherein R is a lower (C₁-C₄) alkyl group or hydrogen, with a base to yield an alkali salt, and liberating the product from said salt with an acid, characterized in that the acidic liberation of the product is carried out above room temperature, preferably in the temperature range of 65 °C to 70 °C.

15 4. A process according to claim 3, wherein a water-miscible organic solvent, preferably aqueous methanol, more preferably methanol containing 20-50 % water by volume is employed.

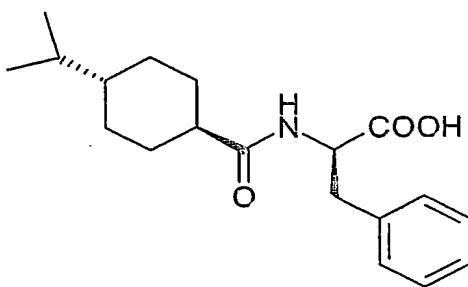
5. Crystals of nateglinide in the "G" form, having

- (a) a melting point of 100 to 109 °C;
- (b) an infra-red spectrum with intensive bands at 1763, 1735, 1614, 1533, 1180, 750, 574 and 491 cm^{-1} ; and
- (c) a Raman spectrum with intensive bands at 1762, 1710, 1182 and 822 cm^{-1} .

6. A process for the preparation of nateglinide in the crystalline modification "H", characterized in that another crystalline modification of the compound having a lower melting point or a mixture of such modifications is boiled in an alkane, preferably in n-hexane or n-heptane for a short time to provide the product in the stable "H" crystalline form.

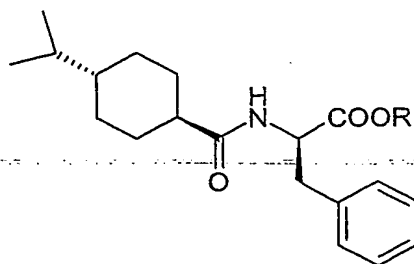
7. A process according to claim 6, characterized in that nateglinide in the crystalline modification "G" is employed as starting material.

8. A process for the preparation of chirally pure N-(trans-4-isopropylcyclohexyl-carbonyl)-D-phenylalanine (nateglinide) of the formula (I)



(I)

by treating a compound of the general formula (II)

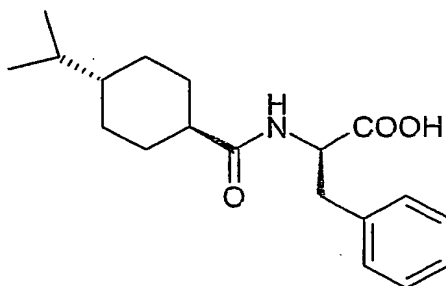


(II)

wherein R is a lower (C₁-C₄) alkyl group or hydrogen, with a base to yield an alkali salt, and liberating the product from said salt with a mineral acid, characterized in that the acidic liberation of the product is accomplished by adding the acid in two portions in such a way that the first time less than equimolar amount of the acid is added to yield a mixture of nateglinide and an alkali salt thereof, said mixture is isolated and a further amount of mineral acid is added to the mixture.

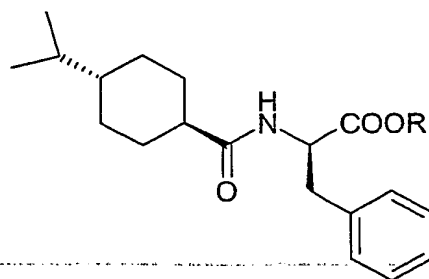
9. A process according to claim 8, wherein a water-miscible organic solvent, preferably aqueous methanol, more preferably methanol containing 20-50 % water by volume is employed.

10. A process for the preparation of crystalline modifications of chirally pure N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide) of the formula (I)



(I)

by treating a compound of the general formula (II)



(II)

wherein R is a lower (C₁-C₄) alkyl group or hydrogen, with a base to yield an alkali salt and liberating the product from said salt with a mineral acid, characterized in that the acidic liberation of the product is accomplished by adding the acid in two portions in such a way that the first time less than equimolar amount of the acid is added to yield a mixture of nateglinide and an alkali salt thereof, said mixture is isolated and further amount of mineral acid is added to the mixture.

11. A process according to claims 1, 3 or 8, characterized in that for liberation of nateglinide from the alkali salt thereof, as the first portion of the acid an amount considering the excess base plus 0.4–0.6 equivalent of the compound of the general formula (II) is employed.